Current concepts in medical practice

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JOHN E. MULLINS, M.D., Editor
Consultant to Hepatic Clinic,
Washington University School of Medicine,
St. Louis, Mo.

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Contributors

Hugh B. Higginbotham, M.D.

Fellow in Cardiology, St. Luke's Hospital, St. Louis, Mo.

G. H. Klinkerfuss, M.D.

Assistant Professor of Neurology, Washington University School of Medicine, St. Louis, Mo.

George A. Koehler, M.D.

Consultant to Arthritis Clinic, Washington University School of Medicine, St. Louis, Mo.

George R. Morrison, M.D.

Assistant Professor and Markle Scholar in Preventive Medicine, Washington University School of Medicine, St. Louis, Mo.

John E. Mullins, M.D.

Consultant to Hepatic Clinic, Washington University School of Medicine, St. Louis, Mo.

Richard B. Oglesby, M.D.

Instructor in Clinical Ophthalmology, Washington University School of Medicine, St. Louis, Mo.

Preface

An editorial note following a volley of correspondence in the *New England Journal of Medicine* (**270**:1072, 1964) states, "it is the *Journal's* hope that the Medical Progress articles will be neither exhaustive nor exhausting." Similarly, the philosophy of the authors of this book is to offer a palatable summation of recent developments without exhausting either the subject or the reader.

The need for such an undertaking seems clear. The population explosion is not limited to *Homo sapiens.* Medical articles and medical journals are also showing a geometric proliferation. The physician laboring under an increasing patient load is likely to be overwhelmed by the increasing literary load.

In this book only the common problems encountered in medical practice are considered. Selections of the literature of about the past two years are displayed in brief form, but include enough background information to render the topic meaningful.

Although the text is well documented with references, the usual tedious practice of parroting every investigator's name has been abandoned. Having a text read like a telephone directory neither honors the diligence of the investigators cited nor renders the style more lucid.

Thus, what follows is designed to be educational and brief. And so may it be.

John E. Mullins,
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Chapter 1

Eye conditions

Richard B. Oglesby

Eye disease, real or fancied, frightens most patients because of its implied threat of blindness. It often frightens the physician as well, because of the mystifying array of instruments and terminology that often attend its diagnosis and treatment. However, the fears of both patient and physician may be moderated by an awareness of the relationship of eye disease to general disease. This chapter will deal with recent advances in ophthalmology which might help the general physician in diagnosis, treatment, or counseling.

GLAUCOMA

Glaucoma is defined as an intraocular pressure elevated enough to cause damage to the optic nerve and loss of visual field. The major advance in the study of glaucoma in the past decade has been a classification permitting more accurate diagnosis and more rational treatment. Apart from congenital glaucoma, which is due to developmental abnormalities, and secondary glaucoma, which follows injury or inflammation, the important differential classification separates open-angle from narrow-angle glaucoma. The diagnosis rests on the anatomic configuration of the angle made by the anterior surface of the iris and the posterior surface of the cornea (Fig. 1).

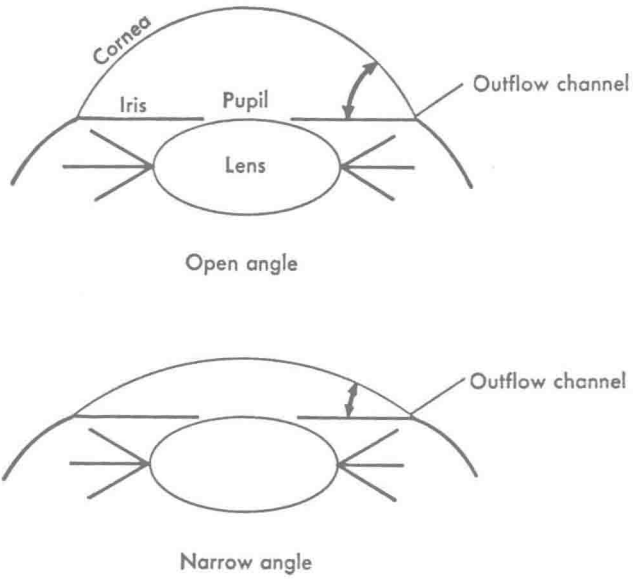

Fig. 1. Types of glaucoma.

Narrow-angle glaucoma

If the angle is narrow, it may close and block the outflow channels for aqueous humor, thereby precipitating acute glaucoma, usually obvious because of unilateral ocular pain, inflammation, and blurred vision. Most clinicians now feel that a surgical opening through the iris, which keeps this angle open, is the treatment of choice in this type of glaucoma.

Open-angle glaucoma

If the angle is open and the pressure is elevated, the blockage to outflow of aqueous lies at a submicroscopic level somewhere between the angle and the veins into which the aqueous ultimately drains. The trabecular meshwork, the first exit for aqueous beyond the angle, has been histologically implicated as a site of such blockage through degeneration and fragmentation of its collagen and proliferation of its endothe-

lial cells. A recent provocative study[1] has shown gamma globulin in this trabecular meshwork in glaucomatous eyes (21 of 25) in contrast to control eyes (6 of 40), thus suggesting that open-angle glaucoma may be a type of connective tissue disease mediated by an antigen-antibody reaction.

The chief reasons for the importance of this type of glaucoma include the following.

1. It is by far the most common type of glaucoma.
2. Its incidence increases with age (2% of the population 40 years of age or more).
3. It remains relatively asymptomatic until advanced loss of visual field has occurred and thus must be detected early by measurement of the intraocular pressure in order to forestall visual loss.

Medical treatment, consisting of cholinergic drugs to promote outflow of aqueous, systemic carbonic anhydrase inhibitors to inhibit its formation, and topical epinephrine, which does both, has been successful in controlling this type of glaucoma, making surgery infrequently necessary.

Detection

Should measurement of the intraocular pressure be a part of every routine physical examination? Becker and Shaffer state: "Intraocular pressures should be measured on all patients old enough to tolerate the procedure, and values over 21 mm. Hg . . . should be considered suspicious and reason for further evaluation."* Pressures greater than 21 mm. Hg occur in less than 2.5% of the normal population and greater than 24 mm. Hg in less than 0.15% of the normal population. In a recent study, 6.4% of the patients reporting to a medicine clinic and surveyed for elevated intraocular pressure proved to have glaucoma on further study.[3] It would appear that such a simple procedure with such a high yield of treatable disease should be a part of a complete physical examination. How-

*From Becker, B., and Shaffer, R.: Diagnosis and therapy of the glaucomas, St. Louis, 1961, The C. V. Mosby Co., p. 59.

ever, it must be emphasized that normal tonometry on one or two examinations does not rule out glaucoma; acute glaucoma may occur in an eye with no previous pressure elevation, and chronic glaucoma is subject to daily variations in pressure. Moreover, one abnormal pressure measurement does not justify telling a patient that he has glaucoma; that diagnosis must be based on changes in the optic disc and characteristic visual field changes as well as on pressure elevation.

Perhaps just as important as routine tonometry in glaucoma detection is a routine question about a family history of glaucoma. A recent report shows the marked tendency of glaucoma to occur more frequently in relatives of proved glaucoma patients. Among 110 close relatives of patients with known glaucoma, 5% had an abnormal intraocular pressure; among those relatives 40 years of age or over, 10% had abnormal pressures—five times the expected rate.[4]

Primary open-angle glaucoma is thought to represent the homozygous state of a recessive gene. The carrier state has recently been identified by a rise in intraocular pressure, the decrease in outflow of aqueous from the eye, and occasionally by the temporary development of characteristic visual field defects during the administration of corticosteroid eye drops. Approximately 30% of "normal" controls, with no overt signs or family history of glaucoma, responded in such a way, indicating a large carrier population.[5]

Systemic implications

Knowledge of glaucoma, of its behavior, and of its implications are important to the general physician for the following reasons.

1. Acute angle closure glaucoma may produce severe headache, nausea, and vomiting with relatively few eye symptoms; thus the eye may be lost while the systemic effects are symptomatically treated.

2. Prolonged use of carbonic anhydrase inhibitors in glaucoma may lead to potassium depletion and its associated symptoms, especially when combined with systemic steroid therapy;

even alone, it may produce anorexia, parathesias, or ureteral colic due to renal calculi.

3. Topical anticholinesterase drugs used in the treatment of glaucoma may cause diarrhea, nausea, abdominal cramps, and weakness. An associated fall in red cell cholinesterase may aid in the differential diagnosis.[6]

4. A sudden lowering of blood pressure may contribute to rapid loss of visual field in patients with early glaucomatous field changes.[7]

5. Topical epinephrine is systemically absorbed and may cause or aggravate cardiac arrhythmias.

6. Hypertonic solutions of urea[8] or mannitol intravenously or glycerol orally are used to lower the intraocular pressure in acute glaucoma. These are effective by increasing the volume of intravascular fluid at the expense of the intraocular and cerebrospinal fluid. The nonprotein nitrogen is temporarily elevated with urea administration. The possibilities of aggravating chronic renal disease, congestive heart disease, or organic psychoses by plasma expansion must be weighed against the known beneficial effects in acute glaucoma.

OPHTHALMOLOGY AND CEREBROVASCULAR DISEASE

Recent advances in the treatment of cerebrovascular disease have quickened the search for reliable diagnostic techniques less morbid than angiography. Ophthalmodynamometry is one of these techniques. It consists of applying a graded external pressure to the eye while observing the effect of this pressure on the retinal arterioles. Diastole is signaled by pulsation and systole by the disappearance of the blood column. The pressure is usually applied to the sclera by a plunger (dynamometer), but recently plethysmographic goggles connected to a manometer have been suggested and would perhaps simplify the technique. Most workers in this field agree that it is best performed by two trained observers—one to apply the dynamometer and one to observe the retinal vessels. Indeed, much unreliable data have accumulated through mis-

applied technique in the hands of the occasional observer. Among patients without eye or neurologic disease, 90% have equal pressures in the retinal arteries, and 10% have differences up to 8 mm. Hg. Hollenhorst concludes that a 10 mm. Hg difference between sides represents pathologic variation.[9] As proved by surgical exploration, dynamometry is 65 to 85% accurate in complete occlusion of the internal carotid artery. In stenosis, dynamometry is helpful in direct proportion to the degree of stenosis. If there is bilateral stenosis, dynamometry is not reliable.[10] Compared to angiography, dynamometry has proved 2 to 25% false-positive and 16 to 35% false-negative[10,11] Thus, in some cases it may be misleading.

Several modifications may increase the sensitivity of this technique. The posture modification compares dynamometric readings in a supine position with those in an erect position; a sudden change to the erect position may uncover a temporarily decreased ophthalmic artery pressure on the side of a partially diseased carotid artery. Similarly, digital compression of a patent carotid artery will produce a marked fall in the ophthalmic artery pressure of both eyes, in contradistinction to compression of a diseased carotid, which will have little effect. It should be noted that carotid compression may be hazardous, and several deaths have resulted from this maneuver. Smith,[12] after extensive experience, concluded, "Ophthalmodynamometry, if done with careful attention to techniques, with reproducible determinations of both systolic and diastolic values and supplemented with carotid compression and posture techniques, appears to have an extremely high diagnostic accuracy."* He feels that in addition to suspected cerebrovascular disease, central retinal artery occlusion and unilateral glaucoma are indications for dynamometry. Orthostatic hypotension too may be studied by dynamometry, the postural change in the ophthalmic artery being diagnostic in some cases in which the brachial artery pressures were inconclu-

*From Smith, J. L.: The ophthalmodynamometric carotid compression test, Am. J. Ophth. 56:369, 1963.

sive[13]. While ophthalmodynamometry is a useful diagnostic technique, it is not yet reliable enough to replace angiography if carotid surgery is contemplated.

Fluorescein injected intravenously may be observed in the retinal circulation by a suitably filtered ophthalmoscope. This has led to another assessment of cerebrovascular patency, the arm-to-retina circulation time. In cases of unilateral carotid occlusion proved by surgery or angiography, this test has been accurate in 60 to 95% of patients in a small series.[14,15] It suffers from some of the same disadvantages as does dynamometry however—three trained observers and special equipment are necessary. It is a useful adjunct and may be applied when pressure on the globe itself is contraindicated or when cardiac arrhythmia makes dynamometry unreliable.

DIABETIC RETINOPATHY

Diabetic retinopathy has blinded 29,000 persons in the United States; this represents 8.4% of all blind persons in this country. Statistical evidence indicates that blindness due to diabetic retinopathy is increasing—for example, New York state reports a rise from 4.5 to 12.7% of all blind persons from 1941 to 1955.[16]

Diabetic retinopathy, for this discussion separated from systemic diabetes, has been ascribed to a multitude of causes. Most workers agree that the capillary microaneurysm constitutes the basic lesion. This lesion may arise through venous obstruction or stasis, abortive neovascularization, loss of neuronal vascular tone, pull of mesodermal strands, and a weak spot in the capillary wall; data have been advanced in support of each of these causes. Recent work[17] using a flat preparation of the retina and trypsin digestion to eliminate nonvascular elements implicates capillary occlusion as the primary event. Selective loss of cells in the walls of the vessels which develop microaneurysms was shown, and thickening of the basement membrane of the vascular endothelium was thought to represent a reparative process. Retinitis proliferans differs histologically by lack of aneurysms; it resembles

neovascularization of granulation tissue elsewhere. By contrast, Bloodworth[18] considers diabetic retinopathy to be "[a] . . . complex degenerative disease of all elements of the retina, probably due to a fundamental metabolic or enzymatic defect of the cells and is not related to vascular supply. . . . Neovascularization occurs in areas of degeneration of retina."*

The basement membrane of vascular endothelium appears to be the key tissue in relating retinopathy to systemic derangement. Most workers agree that this is thickened and often reduplicated in diabetes. Several papers postulate that this change is immunogenic; the supporting data showed gamma globulin[19] and subsequently fluorescent insulin[20] bound to retinal capillary aneurysms and to the basement membrane of ciliary body and iris in eyes with diabetic retinopathy. Retinas from nondiabetics or from diabetics without retinopathy showed no binding. It has been noted that retinopathy is significantly less frequent in diabetics with concomitant rheumatoid arthritis.[21] Perhaps these diseases compete for available antibodies, or perhaps the anti-inflammatory drugs used in rheumatoid arthritis have an "immunosuppressive" effect on retinopathy.

The direct relationship between pituitary activity and diabetic retinopathy is an old observation; recent studies show that growth hormones can produce thickening of the basement membrane of retinal vessels (but not retinopathy) in dogs. Clinical application of these observations in the form of hypophysectomy, a long-established experimental technique for the amelioration of diabetes, has been made in the treatment of diabetic retinopathy. The results of such surgery are difficult to evaluate and must be viewed against the natural history of diabetic retinopathy.

In 209 eyes with diabetic retinopathy of varying severity, vision was classified as good, impaired, or blind; the initially blind eyes were excluded from further study, and follow-up

*From Bloodworth, J. M. B.: Diabetic retinopathy, Diabetes 11:1, 1962.

study of the remainder was made. At the end of 5 years of observing the good eyes, 34% were impaired and 15% were blind; of those eyes classified impaired, 50% were blind. Older patients were more susceptible to visual deterioration. Visual loss did not appear to be influenced by the adequacy or inadequacy of diabetic control.[22]

In another study,[23] which concerned itself with only the proliferative (neovascularization) phase of retinopathy, vision on initial examination was classified good in 47% of 977 cases; 34% were legally blind and 7% totally blind. Good vision was found initially in 34% of maturity onset diabetes and in 67% of the juvenile type. During a mean follow-up period of 2 to 3 years, 41% of 100 juvenile diabetics with initially good vision had progressed to economic blindness. In the maturity onset group, 59% of 56 patients had similarly changed. In 109 patients who developed proliferative retinopathy after the initial examination, 40% progressed to economic blindness in 3 years in the juvenile type and 66% in the maturity onset type. In evaluating these data, the surprisingly optimistic implications deserve emphasis. In contrast to the long-held belief that proliferative retinopathy was usually incompatible with good vision, it is seen that nearly half of the patients with such retinopathy had good vision initially, and of this group, 59% (growth onset) and 23% (mature onset) maintained good vision in a mean follow-up period of 2 to 3 years. A final important and surprising facet of this study revealed 35 cases (10%) of spontaneous arrest of proliferative diabetic retinopathy.

Criteria for hypophysectomy in the treatment of diabetic retinopathy have included severe or progressive retinopathy threatening central vision and advanced neovascularization. Patients have been rejected for macular degeneration, massive vitreous hemorrhage, retinopathy without hemorrhage or with slow progression, advanced renal disease, severe hypertension, or severe peripheral vascular disease.[24,16] A recent well-documented study[24] appears to reflect the typical experience[25] with surgery: of 14 patients operated, 2 died in the